

**REMARKS**

Claims 1-22 were pending in the subject application. Applicants have canceled claims 3, 12, 18, and 20-22 without prejudice to their right to pursue the subject matter of these claims in a later filed application, have amended claims 1, 3-11, 13-16 and 19, and have added new claims 23-51. Support for these claims may be found *inter alia* as follows:

claims 23 and 24 may be found throughout the specification, such as on page 19, lines 29-30, and page 19-20, bridging sentence;  
claim 25-26, on pages 28-29, bridging sentence, and page 29, lines 6-10, Table 5 on page 44, and Figures 14, 15;  
claims 27-29 on page 17, lines 3-6 and Tables 4 and 5;  
claim 30 in originally filed claim 13;  
claim 31 in originally filed claim 8;  
claim 32 and 33, on pages 28-29, bridging paragraph;  
claim 34 on page 29, lines 6-7;  
claim 35, on page 29, lines 10-12;  
claim 36 in originally filed claim 11;  
claim 37 in originally filed claim 19;  
claim 38, in originally filed claim 11;  
claim 39, in originally filed claim 19;  
claim 40, on page 37, line 23-26;  
claim 41 on page 11, line 24-25;  
claim 42, on page 13-14, bridging paragraph;  
claim 43, on originally filed claim 7 and page 23, lines 32-36;  
claim 44, on page 23, lines 24-29, and Figures 9-11;  
claim 45, throughout the specification and in particular page 8, 20-27 and page 13, lines 8-14, pages 28-29, bridging sentence, and page 29, lines 6-10, Table 5 on page 44, and Figures 14, 15;  
claims 46-50, page 19, lines 25-34;  
Claim 51, in originally filed claim 8.

Applicants note that claim 1 has been amended to recite, among other things, more than

one elongator tRNA species charged with a non-naturally occurring amino acid or amino acid analog, and that claim 5 has been amended such that it no longer recites radioactive naturally-occurring amino acids. This amendment does not involve any issue of new matter. Applicants respectfully request entry of the subject amendment such that claims 1, 3-11, 13-17, 19, and 23-51 will be pending. Applicants will address all issues in the order that they appear in the Office Action.

### **1. Restriction Requirement**

The Examiner required election of one of the following groups:

- Group I: claims 1-17 and 19, allegedly drawn in part to a cell-free translation system for generating a peptide product or a peptidomimetic product, a kit comprising the translation system, and a method of generating a peptide product or a peptidomimetic.
- Group II: claim 18, allegedly drawn in part to a peptide or peptidomimetic.
- Group III: claims 20-22, allegedly drawn in part to a method of conducting a drug discovery business using the peptide or peptidomimetic.

A provisional election of Group I was made with traverse by Matthew Vincent on February 11, 2004. The undersigned on behalf of applicants affirms this election. Applicants have elected these claim with traverse, in part, because it would not be any undue burden on the Examiner to search all claims.

### **2. Informalities**

The Examiner objected to the disclosure alleging that the specification recites amino acid and nucleotide sequences, but their sequence identifiers are not indicated. In response, applicants have amended the specification to recite the sequence identifiers. Applicants request reconsideration and withdrawal of this ground of objection.

### **3. Claim Rejections – 35 USC § 112**

The Examiner rejected claims 2, 4, 5, 7-17 and 19 under 35 USC § 112 as allegedly failing to particularly point out and distinctly claim the subject matter which applicants regard as their invention.

"Substantially Free"

Specifically, the Examiner considers the term "substantially free" in claims 2, 4, and 5 to be indefinite. The Examiner alleges that the term "substantially free" is unclear as to whether the preparation contains any amount of the translation factors EF-P, W, W2 or rescue or whether it contains none at all. Applicants traverse the Examiner's rejection. MPEP 2173.05(b) states as follows:

The fact that claim language, including terms of degree, may not be precise, does not automatically render the claim indefinite under 35 U.S.C. 112, second paragraph. *Seattle Box Co., v. Industrial Crating & Packing, Inc.*, 731 F.2d 818, 221 USPQ 568 (Fed. Cir. 1984). Acceptability of the claim language depends on whether one of ordinary skill in the art would understand what is claimed, in light of the specification...The term "substantially" is often used in conjunction with another term to describe a particular characteristic of the claimed invention. It is a broad term. In *re Nehrenberg*, 280 F.2d 161, 126 USPQ 383 (CCPA 1960). The court held that the limitation "to substantially increase the efficiency of the compound as a copper extractant" was definite in view of the general guidelines contained in the specification. In *re Mattison*, 509 F.2d 563, 184 USPQ 484 (CCPA 1975). The court held that the limitation "which produces substantially equal E and H plane illumination patterns" was definite because one of ordinary skill in the art would know what was meant by "substantially equal." *Andrew Corp. v. Gabriel Electronics*, 847 F.2d 819, 6 USPQ2d 2010 (Fed. Cir. 1988).

Applicants respectfully remind the Examiner that, as required in the section of the MPEP recited above, the acceptability of claim language which is allegedly not precise depends on whether one of ordinary skill in the art would understand what is claimed, in light of the specification. Applicants contend that the specification provides sufficient guidance to one of ordinary skill for interpreting the claims. For example, page 16, lines 11-17 state that "A 'reconstituted translation system' refers to a reaction mixture ... characterized by having less than 10 percent of the contaminating proteins found in cell lysate translation systems or wheat germ extract translation systems, and more preferably having less than 5 percent or even less than 1 percent of such contaminating proteins." Furthermore, one of ordinary skill in the art

would appreciate, based on the teachings of the specification, that the translation systems of the invention comprise purified components, and the experiments disclosed in the specification exemplify the purification of such components and their level of purity. Accordingly, applicants request reconsideration and withdrawal of this ground of rejection.

“Peptidomimetic Product”

The Examiner considered claims 4 and 5 to be indefinite because they recited “a peptidomimetic product” while claim 2, from which claims 4 and 5 depend, recited a “peptide product”. In response, applicants have amended claims 4 and 5 to recite a “peptidomimetic product”, thereby obviating this ground of rejection. Accordingly, applicants request reconsideration and withdrawal of this ground of rejection.

“Alkyne Derivative” and “Radioisotope Derivative”

The Examiner considered the terms “alkyne derivative” and “radioisotope derivative” in claim 5 to be indefinite. Applicants traverse this ground of rejection, since one of ordinary skill in the art of chemistry understands what is meant by the alkyne derivative of allyl glycine. Because the phrase “alkyne derivative” does not refer to just any derivative of allyl glycine, but rather to the alkyl derivative, one skilled in the art would know that the alkyl derivative of allyl glycine would correspond to propargyl glycine, and not any other compound. Accordingly, the term has a specific and unambiguous meaning to one skilled in the art. Without conceding the correctness of the Examiner’s argument but to expedite prosecution, applicants have amended claim 5 to replace the phrase “alkyl derivative” with “alkyl counterpart”, and have removed references to a radioisotope derivative. Accordingly, applicants request reconsideration and withdrawal of this ground of rejection.

The Examiner alleges that the term “said inactive tRNA species” in claim 7 lacks proper antecedent basis, and further rejects claims 8 and 10 as being dependent on claim 7 and not correcting this alleged deficiency. In response, applicants have amended the claim to provide proper antecedent basis.

The Examiner alleges that claims 9 and 10 are indefinite because the claims do not recite what the kit is used for or what the instructions are. Without conceding the correctness of the

Examiner's argument but to expedite prosecution, applicants have amended claims 9 and 10 to indicate an intended use for the kit. Support for this amendment may be found, for example, on page 9, lines 9-10, page 31, lines 35-36, and originally filed claim 1. Accordingly, applicants request reconsideration and withdrawal of this ground of rejection.

The Examiner stated that claims 11-17 and 19 are indefinite because the claims allegedly lack an essential step in the generation of a peptidomimetic *i.e.* the implicit step of allowing translation to proceed. In response, applicants have amended claims in accordance with the Examiner's suggestion. Support for this amendment may be found throughout the specification, such as on page 21, lines 17-25. Accordingly, applicants request reconsideration and withdrawal of this ground of rejection.

The Examiner alleges that claims 11 and 19 are indefinite because the claims recite the term "and/or." Applicants have amended claims 11 and 19 to remove the term "and/or." Accordingly, applicants request reconsideration and withdrawal of this ground of rejection.

### **3. Claim Rejections – 35 USC § 102**

The Examiner rejects claims 1-7 under 35 USC § 102 as allegedly being anticipated by Stade et al (Nucleic Acids Res. 22, 1394-1399 (1994)). The Examiner also rejects claims 1, 3, 6, 7, 11 and 12 as allegedly being anticipated by Ganoza et al. (Proc Natl. Acad. Sci. USA 82, 1648-1652 (1985)).

Applicants have amended independent claims 1 and 7. Support for these amendments may be found on page 13, lines 4-7, page 19, lines 26-29, page 28-29, bridging paragraph, page 29 lines 6-7 and 10-12, and page 44, table 5 of the originally filed specification. Support for the term "elongator tRNA" may be found on page 11, lines 23-27, page 27, lines 8-11, and in the experimental examples. Applicants have also amended dependent claims 4-6, 9, 11 and 13-15.

Applicants traverse the Examiner rejections. Applicants respectfully note that in accordance with MPEP 2131.01, to anticipate a claim, a reference must teach every element of the claim. More specifically, this section of the MPEP states that "A claim is anticipated only if each

and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.”

However, neither Stade nor Ganoza teaches every element recited in independent claims 1 and 7. Claim 1, for example, recites at least the following three elements of the translation system:

(a) more than one elongator tRNA species charged with a non-naturally occurring amino acid or amino acid analog;

(b) the capability of translating exogenously added mRNA(s) with highly selective incorporation at each codon;

(c) the capability of forming a peptidomimetic product.

Similarly, the translation system according to claim 7 recites elements (a) and (c), which are also not taught by Stade or Ganoza.

#### A. Stade

According to the MPEP, in order to anticipate claim 1, Stade must teach all three elements recited above, which it fails to do. For example, Stade fails to teach element (a). Stade relates to a translation system which uses a single tRNA species charged with an amino acid analog, more specifically a derivative of methionine or a derivative of lysine. Stade, however, does not teach a translation system comprising two elongator tRNA species charged with amino acid analogs, and therefore does not anticipate claim 1. Applicants further note that the use of a modified initiator methionine tRNA species in Stade does not anticipate claim 1, since claim 1 recites the use of elongator tRNA species.

Stade also fails to teach element (b), a translation system with highly selective incorporation at each codon. Page 17, lines 3-6 of originally filed specification recite that “By “highly selective incorporation at each codon”, it is meant at least 80% selective incorporation. Stade is silent as to the selectivity of the system and does not claim that the system described achieves at least 80% incorporation. Applicants believe that the arguments set forth in the Office Action do not consider this element of the claims, when this element provides yet another point of distinction between the claimed invention and the prior art. For example, Fanestock et al., *Science* 173(994):340-3, cited in the supplemental IDS concurrently filed herewith, describes the

incorporation of just a single aminoacyl tRNA species charged with the phenylalanine analog phenyllactic, uses the tRNA species as an initiator tRNA, while achieving lower selectivity at each codon. By contrast, the claimed invention recites the use of more than one elongator tRNA species and highly selective incorporation at each codon.

Not only does Stade fail to teach all the elements of claim 1, but it fails to teach additional elements recited in several of its dependent claims. For example, claim 5 recites a group of amino acid analogs, none of which are taught by Stade, since Stade only relates to diazirine derivatives of methionine and lysine which are not members of the group. Similarly, claims 6 recites a translation system which further includes more than one exogenously added mRNA species. Stade, however, only teaches the use of a single exogenously added mRNA in the translation system to study the crosslinking of a translation product to a ribosome. Thus, even if the Examiner maintains that Stade anticipates claim 1, which it does not, dependent claims 5 and 6 would not be anticipated since Stade fails to teach the elements which they recite. Finally, Stade also fails to teach the elements of, and thus to anticipate, new added claims which are dependent on claim 1, such as, for example, claims 25-29, 32, 33 and 40-42.

Similarly, independent claim 7 recites both elements (a) and (c) listed above. Since Stade must teach both of these elements to anticipate this claim, and it fails to do so for the same reasons as listed above for claim 1, Stade does not anticipate claim 7 nor its dependent claims, such as claim 31.

Accordingly, applicants request reconsideration and withdrawal of this ground of rejection based on Stade.

#### B. Ganoza

According to the MPEP section recited above, in order to anticipate claim 1, Ganoza must teach all three of the elements recited above. On the contrary, Ganoza fails to teach any of the three elements.

For example, Ganoza fails to teach element (a) *i.e.* a translation system with more than one tRNA species charged with a non-naturally occurring amino acid or amino acid analog.

Ganoza relates to a translation system in which tRNA species contain naturally occurring amino acids, two of which, Met and Lys, are radioactive. However, a naturally occurring amino acid which is radioactive is neither an amino acid analog nor a non-naturally occurring amino acid, and thus Ganoza fails to teach element (a).

Furthermore, even if Ganoza had taught the use of amino acid analogs, which it does not, Ganoza is silent as to the incorporation at each codon, and does not state that the translation system described therein achieves at least 80% selective incorporation at each codon *i.e.* element (b).

Similarly, Ganoza fails to teach element (c), *i.e.* the capability of forming a peptidomimetic product. As described in the preceding paragraph, Ganoza teaches, at most, the generation of a radioactive polypeptide, but not the formation of a peptidomimetic product, and thus fails to teach this element of claim 1.

As was the case with Stade, not only does Ganoza fail to teach all the elements of claim 1, it also fails to teach additional elements recited in its dependent claims. For example, claim 5 recites a group of amino acid analogs, none of which are taught by Ganoza. Accordingly, even if the Examiner maintained that Ganoza anticipates claim 1, which it does not, dependent claim 5 is not anticipated by Ganoza since Ganoza fails to teach the elements which it recites. Finally, Ganoza also fails to teach the elements of, and thus to anticipate, new claims which are dependent on claim 1, such as, for example, claims 25-29, 32, 33 and 40-42.

Similarly, independent claim 7 recites both elements (a) and (c) listed above. Since Ganoza must teach both of these elements to anticipate this claim, and it fails to do so for the same reasons as listed above for claim 1, Ganoza does not anticipate claim 7 nor its dependent claims.

Accordingly, applicants request reconsideration and withdrawal of this ground of rejection based on Ganoza.

### **C. Additional Amendments**